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Comparison of SWAP and SAP on the point of glaucoma conversion

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Ioannis Havvas[1,2]
Dimitris Papaconstantinou[1]
Marilita M Moschos[1]
Panagiotis G Theodossiadis[1]
Vasilios Andreanos[1]
Pantelis Ekatomatis[1]
Ioannis Vergados[1]
Dimitrios Andreanos[1]

[1]Department of Ophthalmology, School of Medicine, University of Athens, General Hospital of Athens, Athens, [2]Department of Ophthalmology, General Hospital of Patras, Patras, Greece

Background: The purpose of this study was to compare the two perimetric modalities, SWAP (short wavelength automated perimetry) and SAP (standard automated perimetry), on the point of conversion to glaucoma.

Methods: In this prospective, longitudinal, follow-up study, 282 patients with ocular hypertension were recruited consecutively and tested with both SAP and SWAP annually for 5 years or until the onset of conversion to glaucoma. SAP and SWAP perimetry was performed with the Humphrey Field Analyzer II using the 24-2 full-threshold test. Abnormality for both SAP and SWAP fields was determined on the pattern deviation plot and defined as either a) one point below the 0.5% probability level or b) a cluster of 2 or more points below 1% or c) a cluster of 3 or more points below 2% or d) a cluster of 4 or more points below 5%. Abnormal tests had to be confirmed on a subsequent test within one year to be classified as conversion.

Results: Of the 282 patients initially recruited, 32 were excluded. Of the 250 remaining patients, a total of 38 converted during the follow-up period; 36.8% of conversions were detected earlier with SWAP, 29% simultaneously, and 34.2% were not detected with SWAP during the follow-up period; 2.4% of patients showed SWAP visual field loss that did not result in conversion during the follow-up period.

Conclusion: The results in our study are inconclusive. There were patients with earlier, simultaneous, or no SWAP conversion, with SAP conversion as the golden standard criterion. One should consider both SAP and SWAP with confirmation when visual field loss is evident to maximize early detection of glaucoma, because it appears that each method identifies early glaucoma in a subset of patients and these subsets overlap only partially.

Keywords: short wavelength automated perimetry, standard automated perimetry, blue on yellow, glaucoma conversion, ocular hypertension

Introduction

Glaucoma is defined as a progressive optic neuropathy that leads to a characteristic visual field loss. It is one of the leading causes of blindness, ranking second worldwide and affecting more than 70 million people globally.[1–3] Approximately half of these people are unaware that they have the disease.[1]

Ocular hypertension is a major risk factor for the development of primary open angle glaucoma, and progression can be slowed by reducing the intraocular pressure.[4] Early diagnosis is key to treating the disease at an early stage. Standard automated perimetry (SAP) has been the gold standard for diagnosis of glaucoma and detection of progression, but is not selective for a particular ganglion cell type. It is often quoted that the death of more than 30% of ganglion cells is needed before SAP is able to detect

Correspondence: Ioannis Havvas
Oinouson 28, Patras 26334, Greece
Tel +30 69 4436 5511
Email havvasioannis@yahoo.gr

the visual field loss.[5] Therefore, SAP is not sensitive enough for early detection of glaucoma. Short wavelength automated perimetry (SWAP) is an alternative perimetric method, that isolates the response of a subpopulation of retinal ganglion cells. SWAP is reportedly more sensitive and may predict conversion to glaucoma years earlier than SAP, but the exact etiology is unknown.[6–10] SWAP has several drawbacks that limit its current utility in the clinical situation. It is more time-consuming and tiring for the patient, has greater variability[11] and fluctuation,[12,13] and is influenced by the condition of the lens in comparison with SAP.[13]

Our study is a prospective, longitudinal, follow-up study of ocular hypertensive subjects with the purpose of comparing the two perimetric modalities, SWAP and SAP, at the moment of conversion to glaucoma.

Materials and methods

The methods and procedures used in this study adhered to the Declaration of Helsinki and all subjects gave their informed consent before participation. The study had the approval of the institutional review board. Two hundred and eighty-two patients with ocular hypertension were recruited consecutively and tested with both SAP and SWAP annually for 5 years or until the point of conversion to glaucoma. Eligible patients had untreated intraocular pressure of ≥22 mmHg by Goldmann applanation tonometry in both eyes on at least two occasions, SAP fields within normal limits on at least two separate occasions, and no other ocular or systemic condition that may have affected their visual fields other than the risk of glaucoma. The appearance of the optic disc was not a selection criterion. The patients were all under the care of a referring physician and decisions regarding treatment were left to the discretion of these parties. The participants took two SAP and SWAP fields within a month and the second was used as the baseline to minimize the learning effect. A normal SAP field was defined as a glaucoma hemifield test within normal limits and no abnormal points in the total or pattern deviation probability plots.

All subjects were of white ethnic origin, had a best corrected visual acuity of at least 6/10, open angles on gonioscopy, and an unremarkable slit-lamp examination. Exclusion criteria were significant coexisting ocular or systemic disease that could possibly affect the visual field (eg, diabetes mellitus), intraocular surgery (except for uncomplicated cataract surgery), arterial hypertension, or any previous use of intraocular pressure-lowering medication within 3 months before recruitment. A family history of glaucoma was not an exclusion criterion.

Both SAP and SWAP were performed with the Humphrey Field Analyzer II (Carl Zeiss Meditec, Dublin, CA, USA) using the 24-2 full-threshold test. For SAP, a Goldmann size III white stimulus (maximal intensity 10,000 asb, duration 200 msec) on a 31.5 asb white background was used. For SWAP, a size V light stimulus was chosen, with a 440 nm wavelength blue spot projected onto a 530 nm wavelength yellow background at a maximal brightness of 100 cd/m^2. During the test, the automatic gaze tracking system was activated and the blind spot fixation was monitored not only with the Heijl–Krakau method but also by an experienced perimetrist. All participants were given the same instructions for the examination to minimize operator bias and were allowed to adapt to the background light for at least 5 minutes before testing. They were given the appropriate near refraction and the order of the tests was the same. Resting periods of 3 minutes were included before each examination and at 5-minute intervals during examination of each eye.

None of the visual fields had a glaucoma hemifield test with generalized depression of sensitivity. No correction was made for possible lens transmission losses. The reliability of each visual field was assessed, and the test was considered reliable only if fixation losses and false positive and false negative rates were less than 25%. For classification and analysis purposes, the values of the total and pattern deviation plot, the glaucoma hemifield test, the mean deviation, and the pattern standard deviation were derived from the visual fields printout and entered into a database. Abnormality for both SAP and SWAP fields was determined on the pattern deviation plot and defined as either a) one point below the 0.5% probability level or b) a cluster of 2 or more points below 1% or c) a cluster of 3 or more points below 2% or d) a cluster of 4 or more points below 5%. The abnormal tests had to be confirmed on a subsequent test within one year to be classified as conversion.

Statistical analyses were performed using Statistical Package for the Social Sciences version 17 software (SPSS Inc, Chicago, IL, USA). All quantitative parameters used in the study were expressed as the mean ± standard deviation. Parametric variables were compared with independent Student's *t*-tests, while the chi-square test was used for proportions. A P-value < 0.05 was considered to be statistically significant.

Results

From the 282 patients initially recruited, 32 were excluded for the following reasons: seven developed fundus pathology (one central retinal vein occlusion, one branch retinal

vein occlusion, four nonproductive diabetic retinopathy, one age-related macular degeneration),15 were not consistent with their follow-up appointments, and 10 developed other confounding conditions (corneal ulcer, visually significant cataract, trauma, neurologic disease). Finally, 250 participants were included. Characteristics of the cohort including age, gender, baseline (untreated) intraocular pressure, spherical error, family history of glaucoma, treatment with antiglaucoma medication, central corneal thickness (CCT), and follow-up period are shown in Table 1. Of these, age, baseline intraocular pressure, spherical error, and family history of glaucoma reached statistical significance ($P < 0.05$). A total of 38 patients (7.6%) converted during the follow-up period. Five patients converted in both eyes simultaneously. SWAP showed earlier conversion in 14 patients. In these patients, SAP conversion followed within 24 months. SWAP reproducible defects not meeting conversion criteria appeared in six more patients, but SAP fields in these patients remained normal or did not meet conversion criteria throughout the study period. In 11 patients, the conversion happened simultaneously. In 13 eyes, SAP conversion occurred before SWAP.

Discussion

The number of subjects with ocular hypertension who converted to glaucoma in our study was 7.6% in 5 years. The 5-year Ocular Hypertension Treatment Study conversion rate was 4.4% in the group treated with antiglaucoma medication and 10.9% in the untreated group,[4] so our result was within the expected range. A significant proportion of our subjects were treated. Moreover, conversion in the Ocular Hypertension Treatment Study was determined using perimetry or disc changes, whereas in our study we examined only the perimetric conversion.

Table 1 Patient characteristics

	Nonconverters (n = 212)	Converters (n = 38)	*P*-value
Age, years	45.54 ± 14.92	51.02 ± 10.04	0.0305*
Gender			
Male	118 (55.6%)	22 (57.9%)	0.9318+
Female	94 (44.4%)	16 (42.1%)	
Intraocular pressure (baseline, untreated), mmHg	25.2 ± 5.1	27.3 ± 3.2	0.0149*
Spherical error	0.48 ± 1.41	−1.12 ± 2.04	<0.0001*
Family history of glaucoma	32 (15%)	14 (37%)	0.0027+
Treated with medication	104 (49%)	20 (53%)	0.7810+
CCT	552 ± 31	555 ± 34	0.5888*
Mean follow-up period, years	4.8 (range 2.2–5.6)		

Notes: *P-value for *t*-test; +P-value for chi-square test; significance level <0.05.
Abbreviation: CCT, central corneal thickness.

The results in our study are inconclusive. There were patients with earlier, simultaneous, or no SWAP conversion, with SAP conversion as the golden standard criterion. To be exact, 36.8% of conversions were detected earlier with SWAP, 29% simultaneously, and 34.2% were not detected with SWAP during the follow-up period. Further, 2.4% of patients showed SWAP visual field loss that did not result in conversion during the follow-up period. The subset of patients with ocular hypertension where SWAP showed earlier or simultaneous conversion with SAP (65.8%) is in line with previous reports.

Numerous studies have established the concept that SWAP can detect glaucomatous visual field changes earlier than standard SAP. They showed that SWAP can be an early indicator of glaucomatous damage, predicts SAP glaucomatous visual loss, and also that the rate of progression of SWAP deficits is more rapid in early glaucoma patients.[6–8,14,15] The subset of patients showing SAP conversion without SWAP conversion is in accordance (albeit to a lesser extent) with the study by van der Schoot et al, where 63% of conversions occurred earlier in SAP.[16] In the published literature, the outcomes of many studies are conflicting. There are many reasons for that:

1. Early studies were based upon relatively small numbers of patients and normal subjects.[6,7,14,17]
2. The built-in normative databases for SAP and SWAP were obtained in separate populations which makes it difficult to make direct comparisons of the procedures. For this reason, some glaucoma researchers have developed normative values for all tests being evaluated for the same population of participants and have followed them longitudinally.[9,18] Soliman et al suggested that the current statistical package and its normative database is flawed and questioned its validity in clinical practice.[19] They concluded that SWAP is less efficient than SAP in detecting visual field defects in patients with glaucoma and ocular hypertension.[19] It is possible that systematic differences between our study group and the normative database could have caused imprecision in estimation of SWAP visual field loss.
3. The visual field abnormalities detected by SWAP are dependent on the criteria that define abnormality. These criteria are not uniform across studies[9,18,20] and it has not been proven which criteria are most reliable.[21] Some studies use criteria for abnormality that had been designed for SAP in clinical trials, but this could lead to errors because of the larger normal intersubject variability in SWAP.

4. Visual field abnormalities need confirmation so that they can be distinguished from chance variability and false positives. In the Ocular Hypertension Treatment Study, 86% of first occurring abnormal visual fields were not confirmed on the next retest.[22] Earlier studies did not make clear whether visual field defects were reproducible.[6] Some of them could have been false positives. One strength of our study is that all visual field loss was confirmed.

Takada et al and Mattos et al showed that SAP using stimulus size I is more sensitive than SWAP (using stimulus size V) in detecting early glaucoma damage.[23,24] Bengtsson and Heijl found that conventional Swedish interactive thresholding algorithm (SITA) fast SAP was not inferior to full-threshold SWAP and SITA SWAP with respect to diagnostic sensitivity.[25]

Examining the functional basis of the proposed SWAP enhanced sensitivity, one can find many contradictory publications. More specifically, three theories have been proposed for the pattern of retinal ganglion cell loss in early glaucoma:

1. A subset of ganglion cells are affected first and in particular higher diameter ganglion cell fibers.[26] However, Yucel et al found no evidence of selective loss in glaucoma within the magnocellular, parvocellular, or koniocellular layers of the lateral geniculate nucleus.[27]
2. All nerve fibers are potentially damaged, so no specific visual pathway is more vulnerable than another.[28,29]
3. Not all eyes are affected in the same way, meaning that no ganglion cell subtype is always affected first in glaucoma.[30] Sample et al pointed out that function selective tests target specific ganglion cell subtypes, reducing the built-in redundancy of the visual system. They proposed that a combination of test types may be more sensitive in revealing early visual field loss and the area of the retina affected first.[31]

There are several limitations to our study:

1. One limitation in earlier studies and in our study is the inclusion criteria used, ie, only patients with normal SAP fields are included and one would expect a few positive SWAP tests just by chance. Also, patients with an abnormal SAP field but a normal SWAP field are missed. Thus, an inherent sampling bias and the misleading conclusion that SWAP field defects always precede SAP defects is introduced. Due to the design of our study, we did not follow the patients with SAP conversion first to identify if and when they showed SWAP conversion. The time frame of such a conversion would be of great interest, given that earlier studies have focused on the prevalence of SWAP visual field loss and the SAP visual field loss that follows.
2. We did not account for the extended learning effect in SWAP. Patients were tested twice with SWAP and the second test was used as baseline. It has been shown that the learning effect in SWAP is more prolonged than in SAP (which actually stabilizes after the fifth test visit) and that experience in SAP is not transferable to SWAP.[32,33] Thus, in patients exhibiting normal results from SAP, some defects identified by SWAP can be attributable to a learning artifact rather than to early damage. However, we did confirm abnormal visual fields with a second test shortly after the first.
3. No correction for possible losses of lens transmission was made. Cataract causes a generalized depression of sensitivity both in SAP and SWAP, but is more pronounced in SWAP.[34] Earlier studies accounted for this.[9,18] However, the criteria applied in our study were points on the pattern deviation plot, which is already corrected for any generalized reduction in sensitivity. Moreover, patients with cataract were excluded. It has also been shown that correction for lens transmission losses does not influence the diagnostic accuracy of SWAP for detecting visual field loss.[34]
4. The appearance of the optic disc was not a selection criterion, and data on the disc were not gathered prospectively. That means that the prevalence of SWAP glaucomatous defects could have been influenced by the different proportion of patients with structural glaucomatous loss (preperimetric glaucoma).
5. We used the full-threshold SWAP and not SITA SWAP. SITA SWAP is an improved version of SWAP, with significantly less testing time (approximately 70%), and an improved normative database which corrects for cataractous lens losses. SITA SWAP, allegedly, has an enhanced ability to detect visual field damage relative to full-threshold SWAP with the greater variability and duration.[31] However, Bengtsson and Heijl concluded that "the SITA SWAP identified at least as much glaucomatous visual field loss as the older full-threshold SWAP, although test time was considerably reduced. Conventional SAP using SITA Fast was not significantly less sensitive than either of the two SWAP programs".[25] Moreover, Ng et al showed that both algorithms are equally sensitive for the same specificity cutoff values.[35]

In conclusion, it appears that the pattern of appearance of visual field loss in SWAP relative to SAP is not consistent

across studies. There are cases in which SWAP visual field loss is not followed by SAP visual field loss over more than 5 years of follow-up evaluations. Sometimes SAP visual field loss occurred at the same time and at times also prior to SWAP visual field loss.[16] There is evidence that a particular location of the retina is affected first in a given person, but the visual function that is the first to fail is not constant.[31,36] Although techniques that rely on structural measurements (optical coherence tomography, Heidelberg retina tomography, laser polarimetry) have gained popularity because they are less patient-dependent and therefore more objective, demonstration of functional loss that corresponds to observed structural changes leads to a more secure diagnosis. It seems that early damage in glaucoma is not the same for every individual (idiosyncratic). Techniques that attempt to improve detection of field loss in glaucoma by selectively stimulating visual pathways with low functional redundancy are not able to identify all patients at risk. More specifically, one should consider both SAP and SWAP with confirmation of the results when visual field loss is evident, to maximize early detection, because it appears that each method identifies early glaucoma in a subset of patients and these subsets overlap only partially.

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Author contributions

The authors alone were responsible for the content and writing of the paper.

Disclosure

The authors report no conflicts of interest in this work.

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